REMARKS

The present invention relates to previously unknown biological roles of Nogo-B.

Claims 39-45 and 49-59 are currently pending in this application. Claims 39-41, 44, 45, and 49-54 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1-38 and 46-48 have previously been canceled. Therefore, claims 42, 43, and 55-59 are currently under consideration.

Claims 42 and 56 have been amended herein. Specifically, claims 42 and 56 have been amended to address the Examiner's concern regarding lack of antecedent basis. Claim 42 has also been amended to indicate that the Nogo-B fragment is an amino terminus fragment of Nogo-B. Support for this amendment is found at least in lines 2-5, page 14 of the as-filed specification. No new matter has been added by way of these amendments.

Rejection of claims 42-43 and 55 pursuant to 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 42-43 and 55 under 35 U.S.C. § 112, first paragraph, as lacking enablement. Specifically, the Examiner contends that the specification does not enable the use of fragments of Nogo-B, other than a fragment of Nogo-B comprising 1-200 amino acids of the amino terminus of Nogo-B, for the treatment of conditions characterized by pathological vascular remodeling. The Examiner is of the opinion that Applicants would have had to perform "undue experimentation" to make and/or use the claimed invention. Applicants respectfully submit that the claimed invention is enabled by the specification as filed under the current law pursuant to 35 U.S.C. § 112, first paragraph, for the following reasons.

As an initial matter, Applicant enjoys a presumption that the specification, which discloses how to make and use the claimed invention, complies with the first paragraph of 35 U.S.C. §112, unless there is a reason to doubt the objective truth of the specification. See, *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). The initial burden of establishing a basis for denying patentability to a claimed invention rests upon the examiner. See, *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Thorpe*, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985); *In re Piasecki*, 745 F.2d 1468, 223 USPQ 785 (Fed. Cir. 1984).

It is well-settled that an Applicant need not have actually reduced the invention to practice prior to filing. MPEP §2164.02 (citing *Gould v. Quigg*, 822 F.2d 1074 (Fed. Cir. 1987)). Indeed, the invention need not contain an example if the invention is otherwise disclosed

in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908 (C.C.P.A. 1970). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. MPEP §2164.01 (citing *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976)). The fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. *Id.* Further, the specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. MPEP §2164.05(a) (citing *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991)). Therefore, under current law, enablement does not require a working example and experimentation is allowed so long as it is not undue. The present case law regarding enablement under 35 U.S.C. §112, first paragraph, allows significant experimentation without finding it undue if the art typically engages in such experimentation.

Applicants submit that the present Experimental Examples, taken in view of the specification, provide abundant guidance to the skilled artisan to practice the claimed invention. In addition, the claims have been amended herein to indicate that the composition comprises Nogo-B or an amino terminus fragment of Nogo-B. Support for this amendment is found at least in lines 2-5, page 14 of the as-filed specification.

The present invention is based on the discovery of the novel role of Nogo-B and an amino terminus fragment of Nogo-B in adhesion, spreading and migration of endothelial cells. The inventors identified Nogo-B and the amino terminus fragment of Nogo-B as a component of caveolin-1 enriched membranes (CEM) and "lipid rafts" (LR). As set forth in the Background section, CEM/LR have been implicated in a variety of biological functions including signal transduction. The inventors identified Nogo-B and an amino terminus fragment of Nogo-B as a novel regulator of vascular homeostasis and remodeling.

Armed with the disclosure of the specification relating to a biologically active amino terminus fragment of Nogo-B and what was already known in the art, the skilled artisan would not have had to engage in any undue experimentation to practice the invention commensurate with the scope of the pending claims directed to a biologically active amino terminus fragment of Nogo-B. This is because the skilled artisan, armed with the teachings provided in the application as filed, would have been able to determine, through routine

experimentation, any appropriate amino terminus fragment of Nogo-B useful for regulating vascular homeostasis and remodeling.

The specification discloses various methods of screening and determining the biological activity of Nogo-B and fragments thereof. A skilled artisan armed with the role of Nogo-B in regulating vascular homeostasis and remodeling, and assays provided in the application as filed, would have been able to determine, through routine experimentation, any fragment of Nogo-B having the desired biological activity. Thus, where methods for assessing the utility of the claimed compositions are well known in the art and/or disclosed in the specification, and where the compositions to be tested are properly described (*e.g.*, amino terminus fragments of Nogo-B), it would not be undue experimentation to screen for amino terminus fragments of Nogo-B which have the disclosed utility where the art typically engages in such experimentation.

Thus, where one skilled in the art would have routinely screened various biological activity of Nogo-B fragments to determine their effects on vascular cell function following the teachings of the disclosure provided in the specification as filed, such experimentation would not have been undue even if it was complex. Examples 2, 3, 4, and 9 describe assays for assessing effects of Nogo-B and fragments thereof in the context of cell spreading, cell adhesion, cell migration, and vessel remodeling, respectively. Armed with the teachings of the instant invention and what was already known in the art, the artisan would not have had to engage in any undue experimentation to practice the invention commensurate with the scope of claims 42-43 and 55 and these claims are therefore enabled under 35 U.S.C. §112, first paragraph.

For the reasons discussed above, claims 42-43 and 55 are amply enabled by the specification as filed. Therefore, the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of enablement, should be reconsidered and withdrawn.

Response to Rejection Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected claims 56-59 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner contends that there is no antecedent basis for the phrase "the step of administering" in claim 56. Accordingly, Applicants have deleted the phrase "the step of" from claims 42 and 56. Claims 42 and 56 now recite a "method comprising

administering a composition". Applicants submit that the rejection of claims 56-59 under 35 U.S.C. § 112, second paragraph, is now moot and should be withdrawn.

The Examiner has also rejected claim 59 under 35 U.S.C. § 112, second paragraph, because the Examiner contends that it is unclear as to the metes and bounds of the term "injury". Applicants respectfully disagree with the Examiner's contentions.

It is settled law that the "patent law allows the inventor to be his own lexicographer." *Chicago Steel Foundry Co. v. Burnside Steel Foundry Co.*, 132 F.2d 812 (7th Cir. 1943). *See also* MPEP § 2173.01. This is because "[t]he dictionary does not always keep abreast of the inventor. It cannot. Things are not made for the sake of words, but words for things." *Autogiro Co. v. U.S.*, 155 USPQ 697 (Ct. Cls. 1967). Further, applicant is entitled to have the claims construed in connection with the other parts of the application. *See Autogiro Co. v. U.S.*, 155 USPQ 697 (Ct. Cls. 1967). Therefore, Applicants are entitled to define terms to describe their invention and the claims must be interpreted in light of the other parts of the application including the disclosure in the specification and the definitions provided therein.

Applicants respectfully submit that the specification as filed makes clear the meaning of "injury" in the context pathological vascular remodeling. The specification discloses that blood vessels undergo alterations to various phenomenon, e.g., injury or disease. Thus, "injury" as used in the specification is understood to mean any event that results in alteration of blood vessels. The specification discloses that alterations are accomplished by either outward or inward remodeling of the vessel. Outward remodeling increases the vessel diameter, while inward remodeling decreases lumen diameter. Remodeling also occurs under pathological conditions such as hypertension and in response to injury as in atherosclerosis (an inflammatory process by which the intima becomes thickened with lipid rich gruel and connective tissue), restenosis (a re-narrowing of the vessel lumen), and luminal stenosis after transplant vasculopathy.

One skilled in the art would have understood, based upon the disclosure provided in the specification as filed, that injury to blood vessels encompasses any phenomenon that requires alteration of blood vessels. The specification also discloses that injury to blood vessels can be from pathological conditions such hypertension, restinosis, transplant vasculopathy, arteriosclerosis, ischemia, hypertension, pulmonary hypertension, asthma, vascular infarctions including myocardial infarction.

Applicants point out that it is appropriate to compare the meaning of terms given in technical dictionaries in order to ascertain the accepted meaning of a term in the art. *In re Barr*, 444 F.2d 588, 170 USPQ 330 (CCPA 1971). Webster's dictionary defines "injury" in the context of the medical art as damage to the body. Accordingly, a skilled artisan when armed with the specification would not be confused as to the meaning of "injury". This is because a skilled artisan would understand that an injury would be any damage to the blood vessel that would require vascular remodeling.

For all of the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the Examiner's rejection to claims 13-17 under 35 U.S.C. §112, second paragraph.

Summary

Applicant respectfully submits that each rejection of the Examiner to the claims of the present application has been overcome or is now inapplicable, and that the claims are now in condition for allowance. Reconsideration and allowance of these claims is respectfully requested at the earliest possible date.

Respectfully submitted,

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